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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/631,637	08/02/2000	Jean Gosselin	2097/49123	8660

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CROWELL & MORING, LLP
INTELLECTUAL PROPERTY GROUP
P. O. BOX 14300
WASHINGTON, DC 20044-4300

EXAMINER	
WINKLER, ULRIKE	
ART UNIT	PAPER NUMBER
1648	11

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/631,637	GOSSELIN ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3, 5-56* is/are pending in the application.

4a) Of the above claim(s) *11-15 and 20-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-10 and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Amendment filed May 30, 2002 (Paper No. 10) in response to the Office Action of January 30, 2002 is acknowledged and has been entered. Claim 4 has been cancelled. Claims 1-3, 5-10 and 16 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Applicants arguments regarding the traversal of Group I-III is acknowledge, upon review and reconsideration the following new Election/Restriction Requirement is made:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-16 and 17-19 drawn to a method of treating an infection with bpV in combination with an antiviral compound, classified in class 424, subclass 9.2.

II. Claims 1, 20 and 21, drawn to a method of treating an infection with a combination of bpV and an immunomodulator compound, classified in class 424, subclass 85.4.

III. Claims 22-35, drawn to a method for the enhancement of antimicrobial efficacy of antimicrobial agents with bpV, classified in class 435, subclass 32.

IV . Claims 36-54 drawn to a composition with bpV, classified in class 424, subclass 646.

V. Claims 36, 55 and 56, drawn to a composition of bpV and an immunomodulator, classified in class 530, subclass 351.

Claim 1 links inventions I and II. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim, claim 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim 36 links inventions IV and V. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim, claim 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction

requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Groups IV and V are compositions and are distinct from groups I-III which are drawn to methods. Groups IV and V are compositions and each is distinct from the other because they contain different materials. Group IVcomprises bpV and an antiviral compound in conjunction with a pharmaceutical carrier. Group V comprises bpV and an immunomodulator in conjunction with a pharmaceutical carrier. Though there may be overlap for groups IV and V, the search for one group will not be coextensive with that of the other group.

Groups I-III are drawn to methods and each is distinct from the other because they utilize different starting materials, therefore the outcomes are not be expected to be the same. Group I is drawn to a method of treating an infection with a combination of bpV and an antiviral agent. Group II is drawn to a method of treating an infection with a combination of bpV and an immunomodulator. Group III is drawn to a method of enhanhing the antimicrobial activity of a compound with bpV. The method of Group I-II use different material compositions from the other methods, in addition, the methods treat different infections thereby setting the groups apart from each other.

Additionally, Groups I and IV contains claims directed to the following patentably distinct invention, applicant is required to pick a single disclosed invention for Group I or V:

i. DNA virus, classified in class 424, subclass 229.1.

i. RNA virus other than retrovirus, classified in class 242, subclass 216.1.

iii. Retrovirus, classified in class 424, subclass 187.1.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, because these inventions are distinct for the reasons given above and the search required for one group is not required for another group, restriction for examination purposes as indicated is proper.

Additionally, Groups I, III and IV contain claims directed to the following patentably distinct species of the claimed invention:

1) Human
2) Ovine
3) Bovine
4) Equine
5) Caprine
6) Porcine
7) Feline
8) Canine

The species are phenotypically and genotypically distinct. The examination of species 1-8 in the method parameters would require different searches in the scientific literature and would involve the consideration of separate issues in determining patentability.

Additionally, Groups I, III and IV contain claims directed to the following patentably distinct species of the claimed invention:

1) Intravenously
2) Subcutaneously
3) Intradermally
4) Transdermally
5) Intraperitoneally
6) Orally
7) Topically

The examination of species 1-7 in the method parameters would require different searches in the scientific literature and would involve the consideration of separate issues in determining patentability.

Additionally, Groups I, III and IV contain claims directed to the following patentably distinct species of the claimed invention:

1) Patch
2) Implant
3) Inhalation
4) Aerosol spray
5) Powder
6) Liposomal composition
7) Tablet

The examination of species 1-7 in the method parameters would require different searches in the scientific literature and would involve the consideration of separate issues in determining patentability.

Additionally, Groups I and V contain claims directed to the following patentably distinct species of the claimed invention:

1) Nucleoside analogs
    a. AZT
    b. 3TC
2) Protease inhibitor
3) Neuramidase inhibitor
4) Interferon alpha
5) Non-nucleoside inhibitor

The species differ in their physical, immunological properties and activity in the viral life cycle and are distinct and unobvious in view of each other and are therefore patentably distinct.

Additionally, Group III contains claims directed to the following patentably distinct species of the claimed invention:

1) Nucleoside analogs
2) Protease inhibitor
3) Neuramidase inhibitor
4) Interferon alpha
5) Non-nucleoside inhibitor
6) Non-nucleoside reverse transcriptase inhibitor (NNRTI)
7) Chemokines
8) Chemokine antagonist

The species differ in their physical, immunological properties and activity in the viral life cycle and are distinct and unobvious in view of each other and are therefore patentably distinct.

Additionally, Groups II and V contain claims directed to the following patentably distinct species of the claimed invention:

1) Leukotrienes
2) Chemokines
3) Cytokines
4) Growth factors
5) Interferons

The species differ in their physical, immunological properties and are distinct and unobvious in view of each other and are therefore patentably distinct.

During a telephone conversation with J.D. Evans on August 5, 2002 a provisional election was made with traverse to prosecute the invention of Group I, claim 1-19, with the species election retrovirus, human, oral administration and tablets. Affirmation of this election must be made by applicant in replying to this Office action. Claim 11-15 and 20-56 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Therefore, claims 1-3, 5-10 and 16-19 are currently examined.

Drawings

Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see Notice of Draftsperson's Review form PTO-948.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

Claim Rejections - 35 USC § 112

The rejection of claims 1, 4, 6-10 and 16 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of applicants amendment to claim 1, the claim is now drawn to inhibition of a viral infection.

The rejection of claims 1-3, 5-10, 16-19 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention **is maintained** for reasons of record. Note that claims 2, 3 and 5 are now included in the rejection in view of the amendment to claim 1 and the addition of claims 17-19 which are in view of the new Election/Restriction requirement.

Applicants arguments presented in paper No. 10 have been considered but are not persuasive. Applicant makes the unsubstantiated assertion that "it is known in the art to apply techniques perfected in cell or tissue culture on humans and other mammalian treatment subjects." In a statement made by Joanne Schellenbach, spokeswoman for the American Cancer Society, regarding a study finding (see Washington Times Article by Joyce Howard Price, November 16, 2001, p. 3) she noted that "results of animal studies cannot always be easily replicated in humans." In fact, she said, "not a large percentage" of promising results in animal studies "pan out" for use in humans.

For example inhibiting the replication/infection of a virus *in vitro* with a compound the would not provide evidence that the compound would inhibit the intact virus from infecting its target cell *in vivo*. The example of suramin, this drug was shown to be very promising in *in vitro* studies to block the infectibility of HIV [see Mitsuya et al. Suramin protection of T Cells *in vitro* against infectivity and cytopathic effect of HTLV-III. Science, (1984) Vol. 226, pp.172-174.]. Further study using suramin as an anti-AIDS drug contradicted the results expected from the *in vitro* tests. Sandström et al. [Inhibition of Human T-cell lymphotropic virus Type III in vitro by phosphonoformate. Lancet (1985) Vol. 1, pp.1480-1482.] teach that *in vivo* experiments

demonstrate no significant clinical or immunological improvement and the net effect of suramin was harmful. Therefore, the use of *in vitro* tests is not accepted as an indicator of *in vivo* activity.

In another *in vivo* vs. *in vitro* model passaged U-937 human leukemic cells behaved differently (see Chomienne et al., Discrepancy between *in vitro* and *in vivo* passaged U-937 human leukemic Cells: Tumerorigenicity and sensitivity to differentiating drugs. In Vivo, 1988) when these cells are passage *in vitro* or *in vivo*. Passageing the U-937 cells in mice resulted in the cells losing the ability to differentiate when exposed to differentiating drugs (see Figure 6). The authors were not able to explain this in dedifferentiation phenomenon for leukemic cells, but it is clear that host factors play an important role, either in selecting pre-existing less differentiated cells or by inducing modifications in the cells' proliferation/differentiation status (see p. 286, column 1, 1st paragraph).

The specification does not provide sufficient guidance for the inhibition of a viral infection in a patient infected with HIV with a peroxovanadium. The examples provided in the specification (see figures) are in direct conflict with what is known in the prior art. The prior art indicates that treating HIV infected cells with peroxovanadium compounds causes activation of HIV transcription from the LTR (Barbeau et al., Journal of Biological Chemistry, 1997, see abstract and figure 1). The prior art also discloses an increase in the reverse transcriptase activity in the supernatant indicating that the treatment with peroxovanadium compounds results in an increase in particle release (see 8 and 9). Therefore, in light of the prior art it is not straight forward process to go from *in vitro* data to an *in vivo* treatment in combination with the information that the *in vitro* data presented in the present specification contradicts what is known

in the prior art makes the instantly claimed invention highly unpredictable. Thus, the lack of working examples regarding treatment of any retroviral infection including HIV in a patient, the lack of guidance in the specification, and the unpredictability regarding extrapolating *in vitro* data to an *in vivo* treatment method greatly reduces the probability that one of skill in the art would successfully obtain the claimed invention without undue experimentation. The rejection **is maintained**.

Claim Rejections - 35 USC § 102

The rejection of claims 1-3, 5 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Oliver et al. (Journal of Biological Chemistry, 1998) **is withdrawn** in view of applicants amendments indicating that the infection is now caused by a virus.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ulrike Winkler, Ph.D.

James C. Housel 8/9/02
JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600